U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

PB-251 874

ENVIRONMENTAL CONTAMINATION FROM HEXACHLOROBENZENE

ENVIRONMENTAL PROTECTION AGENCY

20 JULY 1973

113049

EPA 560/6-76-014

PB 251 874

ENVIRONMENTAL CONTAMINATION

FROM

HEXACHLOROBENZENE

APRIL 1976

OFFICE OF TOXIC SUBSTANCES
U.S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U. S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1 REPORT NO	2	3 RECIPIENT'S ACCESSION NO
EPA 560/6-76-014		

4 TITLE AND SUBTITLE	5 REPORT DATE
Environmental Contamination from Hexachlorobenzene	April 1976
	6 PERFORMING ORGANIZATION CODE
7 AUTHOR(S) Early Warning Branch Office of Toxic Substances	8 PERFORMING ORGANIZATION REPORT NO
9 PERFORMING ORGANIZATION NAME AND ADDRESS U.S. Environmental Protection Agency Office of Toxic Substances 401 M Street SW Washington, DC 20460	10 PROGRAM ELEMENT NO 11 CONTRACT/GRANT NO
12 SPONSORING AGENCY NAME AND ADDRESS U.S. Environmental Protection Agency Office of Toxic Substances 401 M Street SW Washington, DC 20460	13 TYPE OF REPORT AND PERIOD COVERED Final 7/20/73 14 SPONSORING AGENCY CODE

15 SUPPLEMENTARY NOTES

16 ABSTRACT

A series of episodes around the world resulted in recognition of the fact that man and his environment are being exposed to Hexachlorobenzene (HCB). The finding of grossly elevated levels in domestic animals, such as at Geismar, Louisiana, elicited the attention of local State, and Federal officials.

This report summarizes available information in the production, use, and toxicity of HCB and presents conclusions and activities undertaken to gain a fuller understanding of the problems associated with this substance so as to formulate a regulatory posture on this toxic substance.

17 KEY WORDS AND DOCUMENT ANALYSIS

DESCRIPTORS	IDENTIFIERS/OPEN ENDED TERMS	COSATI Field/Group
Hexachlorobenzene (HCB)	Env. Analysis Usage Hazard Assessment Contamination	

i

PRICES SUBJECT TO CHANGE

18 DISTRIBUTION STATEMENT	19 SECURITY CLASS (This Report)	21 NO. OF PAGES
Release Unlimited	Unclassified	34
	20 SECURITY CLASS (This page)	22 PRICE
	Unclassified	$4.00-2.25

EPA Form 2220-1 (9-73)

Document is available to the public through the National
Technical Information Service, Springfield, Virginia 22151

EPA 560/6-76-014

ENVIRONMENTAL CONTAMINATION FROM HEXACHLOROBENZENE

by the

EARLY WARNING BRANCH
OFFICE OF TOXIC SUBSTANCES

U.S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

July 20, 1973

PREFACE

The following report, prepared by the Office of Toxic Substances in July 1973, represents the first Agency aggregation of data concerning the problems associated with environmental exposure to hexachlorobenzene. The plan of action by the Environmental Protection Agency and other Federal and State agencies to gather even more data for regulatory decision-making has now been implemented. Even though this document is somewhat out of date, demand for it has been constant over the past two years; it is therefore being made generally available to the public.

TABLE OF CONTENTS

Summary	1
Contamination of Cattle in Louisiana	3
National and International Dimensions of the Program	7
Chemistry and Analysis of Hexachlorobenzene	11
Toxicology Aspects of Hexachlorobenzene	13
Guidelines for Permissible Residue Levels	19
Conclusions and Current Activity	22
Bibliography	26

Summary

Recent discovery of hexachlorobenzene (HCB) in the fat of animals brought to slaughter has focused attention on the hazards of this material. The most serious case involved cattle in central Louisiana. Other incidents of HCB contamination in the past year have involved sheep in western Texas and in eastern California. Sources of HCB in Louisiana appear to be airborne emissions of manufacturing plants which produce chlorinated hydrocarbons and waste disposal practices of these plants. The Texas and California situations have been associated with pesticides which were contaminated with HCB.

Hexachlorobenzene is a stable and persistent chemical. A solid at normal temperatures, it sublimes (vaporizes) rather readily. It is only very slightly soluble in water.

An epidemic of HCB poisoning in man occurring in Turkey in the 1950's was associated with consumption of treated wheat containing 20 ppm HCB. Up to 5000 cases of a condition called porphyria cutanea tarda resulted. In addition to disturbance in porphyrin metabolism, clinical manifestations of photosensitization, hypertrichosis (abnormal hair growth), hepatomegaly (enlarged liver), weight loss, and enlargement of the thyroid gland and lymph nodes were reported.

Appreciable residues of HCB have been found in wild and domestic animals from a variety of locations in North America. It has also been detected in municipal water supplies in the United States.

The largest source of HCB is the waste stream (byproducts) from the manufacture of chlorine and many chlorinated hydrocarbons. It is also a registered fungicide, and is a major impurity in some pesticides, specifically dimethyl tetrachloroterephthalate (Dacthal) and pentachloronitrobenzene (PCNB). Two domestic producers of HCB for sale have been identified, Dover Manufacturing and Stauffer Chemical. In the past, HCB had been an intermediate for production of pentachlorophenol, but apparently this process has not been used in this country for several years.

Existing Federal controls over HCB are very limited, and stem from its registration as a fungicide. Because of this registration, the government can move against foodstuffs contaminated with HCB. However, there are no controls on the industrial use of the material nor on methods of disposal for waste HCB.

The large number of potential sources of HCB and their geographic dispersion suggest that HCB contamination may be a national problem. Despite serious current problems in a few localities, indications are that HCB has not yet reached environmental levels on a broad scale that will cause serious health or food-supply problems. This does not mean the threat is not serious, but rather that we have caught it early enough that preventive measures may still be effective.

Contamination of cattle in Louisiana

The incident in Louisiana came to light when routine fat samples from beef carcasses for pesticide analysis were taken from the Stevens Meat Company by the U.S. Department of Agriculture on December 12, 1972. The laboratory analysis revealed the presence of 1.52 ppm hexachlorobenzene. Three additional cattle from the same herd from the Darrow, Louisiana, area were then slaughtered and tested. All carcasses were condemned because of excessive residues.

The Department of Agriculture was using a guideline of a maximum of 0.3 ppm HCB in fat as a basis for passing carcasses. This value had been set some years previously, but prior to 1972 it had not been necessary to invoke it with regard to domestic meat products. The basis for the figure is not clear, but it appears to have been set by analogy to the acceptable levels for dieldrin.

Since the very high HCB residues found could not be associated with any malpractice on the part of the rancher involved, USDA proposed placing a "hold order" prohibiting the shipment of beef from Louisiana unless each animal was tested for HCB residue. In order to prevent this, the Louisiana Department of Agriculture established a quarantine area covering parts of Ascension and Iberville Parishes just south of Baton Rouge. None of the animals in the areas could go to slaughter without pre- or post-slaughter evidence that they did not contain violative residues of HCB. The area quarantined centered on Geismar, La. It included the part of Ascension parish that is south and west of U.S. highway 61; and that part of Iberville parish bounded by highway 1 on the southwest portion, then northwest on highway 1 to Bayou Gorda, then a line following highway 405 northeast through St. Gabriel until i intersects highway 61.

Since HCB is registered for use as a fungicide seed treatment, an investigation was undertaken by the Pesticide Branch of EPA in Region VI. This involved determining that (1) the high residues found in the cattle were not due to a fungicidal use since the cattle were grass fattened and no supplemental feed was used,

(2) high concentrations of HCB in the soil, grass and air had been detected, (3) HCB is a normal byproduct of perchlorethylene production as well as the production of chlorine using graphite anodes. The tarry residue from perchlorethylene and carbon tetrachloride production reportedly contains 10-15% HCB.

It was estimated that there were 20,000 cattle in the quarantine area and 25,000 immediately to the south. It was suspected that about half of the latter may have been contaminated at the same levels as in the quarantine area. Assumption was also made that the split between calves and adult cattle was 50/50.

A cooperative program, involving EPA, USDA, the state Department of Agriculture, and the state Extension Service, for the survey of the area in Ascension and Iberville Parishes which had been quarantined was undertaken in April, 1973. Biopsy fat samples were collected from cattle within the quarantine area to determine the status of the herds as this affected restrictions placed on their movement to slaughter. These were supplemented by soil, grass, and surface water samples taken from the involved pastures. For these purposes, a field headquarters office was established in Gonzales.

Under the scheme established, three cows and three calves were sampled from each herd. If all six animals showed acceptable HCB levels, the herd would have been released from quarantine and could be shipped without restriction. Animals from herds under quarantine could be shipped only if the particular animal was analyzed for HCB (either before or after slaughter) and showed an acceptable level (less than 0.3 ppm in fat) of HCB. Unfortunately, most herds involved were small, and did not have six animals suitable for biopsy, cancelling any chance that they could be released under this system.

There have been 555 animals tested from 157 herds. Fat samples above 0.5 ppm were found in 29% of the cattle and 84% of the herds.

In response to USDA's petition of April 3, 1973, to establish an official tolerance for HCB, EPA recommended an action guideline of 0.5 ppm on June 1, 1973. This is discussed further below.

Since the action level guideline was set the quarantine area has been reduced to parts of Ascension parish, leaving about 5,000 cattle in the quarantine area. Those herds which were previously tested and shown to be free of contamination are now free from quarantine. USDA has recommended that herds may be released from quarantine if the composite of ten animals tested from the herd is no greater than .35 ppm. If it is known that any animals are over 3.0 ppm they must be included in the sample first. Those known to be between 0.5 and 3.0 must then be included. The remaining animals to make ten may be a random sample. The USDA feels they have 95% confidence that at least 15% of the herds will be in violation using this method. Calves can be released to go to feeder lots if in a three-animal sample no animal is greater than 1.5 ppm. This allows for a dilution factor.

Individual biopsies will permit any individual animal to go to slaughter even if the herd level is violative.

However, the administration of the quarantine is the responsibility of the State Department of Agriculture. USDA can test only carcasses after slaughter, and if the animal is in violation, it cannot be reclaimed by the owner for other purposes. The local county agent has indicated that due to the expense and the fact that they had difficulty obtaining animals with enough fat to sample, three cows and three calves from each herd are being sampled as previously. The highest value of those tested would be the HCB level assigned to the herd to determine if the herd could be freed from quarantine.

It has been realized that the air sampling techniques used by the Louisiana State Air Control Commission and by private contractors last winter did not give samples that accurately reflected the concentrations of HCB in the air. An improved sampling technique was developed at the EPA Perrine Laboratory and is now being used by the State and by EPA Region VI.

It was suspected that disposal of HCB-containing "hex" waste from a perchlorethylene plant in the area may have been a major source of HCB to the environment. The cattle with the highest concentrations of HCB in their fat were located along the 12-mile road which open trucks purportedly traversed with "hex" waste from the plant to the dump. Results of analyses of soil samples taken near the end of April from this landfill showed concentrations of 5000 ppm HCB. Air samples taken at the landfill on May 14 using the new technique showed concentrations in the air of 14 ppb or 16 micrograms/cubic meter.

In the June 4, 1973, status report of hexachlorobenzene emissions, the Louisiana Air Control Commission and the Division of Health Maintenance and Ambulatory Patient Services indicated that they had listed and reviewed the records of all possible HCB sources which may have contributed to the environment of the cattle in the quarantined areas. On-site inspections of all suspect facilities were made, and the list was limited to those capable of being the source of HCB. The remaining list includes Vulcan Materials, BASF Wyandotte, Ascension Parish Sanitary Landfill (Darrow), Monochem, Uniroyal, Stauffer Chemical, CIBA-Geigy, Browning-Ferris Landfill, and Rubicon. These will be required to provide emission test data from their installations.

The Louisiana Air Control Commission at a special meeting on May 30, 1973, moved to "...initiate action aimed at legal proceedings to issue a cease and desist order and if possible go into emergency cease and desist to those industries who are emitting this material, hexachlorobenzene, for any amount, setting a zero tolerance and that this be based on the Air Control Commission Statutes, Section 2202, Sub-Section C, until such time as standards for hexachlorobenzene be established by this Commission to regulate emission for this material."[1]

The Louisiana Air Control Commission and EPA Region VI are continuing to collect air samples in attempts to determine sources. The EPA Mississippi Test Facility has been authorized to do analyses of samples that Region VI has been obtaining.

---

1. Status Report Hexachlorobenzene Emissions in Geismar, Louisiana Vicinity 4 June 73, Louisiana Air Control Commission and Louisiana Department of Health Maintenance and Ambulatory Patient Services.

National and International Dimensions of the Problem

Besides the incident in Louisiana, sizeable numbers of violative sheep have been found in California and in Texas. (The sheep taken to slaughter in Texas were actually raised in New Mexico.) Additionally, numerous positive but "non-violative" findings of HCB have been reported in virtually all kinds of meat animals from many parts of the country. There are large numbers of such reports from California and Colorado, but many other states are also represented. All of these have been found since July, 1972, when USDA first started checking animals for HCB residues.

These samples were taken in USDA's statistically designed spot checking program. In a given year, this program actually involves only small fractions of the animals marketed and of the slaughterhouses in the country.

The Food and Drug Administration's "market basket" surveys have also detected HCB, but generally at low levels. Worrisome residues have been found in some samples of butter and cheese, however. The data do not demonstrate any clear trends. Because of the nature of the survey, the significance of these findings is hard to assess.

As more data from ongoing surveys of agricultural products conducted by USDA and FDA become available, we will be better able to judge the magnitude and extent of HCB contamination of the food supply.

The three most serious incidents (in Louisiana, New Mexico, and California) are currently under investigation. In Louisiana, the source of HCB is almost certainly industrial byproducts; in New Mexico and California, HCB residues appear to result from the use of the herbicide Dacthal, which contains HCB as an impurity. Samples of Dacthal obtained in California contained up to 10% HCB. There is presently no evidence linking HCB contamination of food to the approved use of HCB as a fungicidal seed treatment.

Fungicidal treatments of seed grains such as wheat, barley, oats and rye are the most important pesticidal uses of HCB. The major use is to control bunt in wheat. A typical rate of application for seed treatment is

about 1-3 ounces of a 30% dust per bushel of wheat seed equivalent to 330-990 ppm on the seed. Minor uses include seed treatments for onions and for sorghum. Technical grade materials used for fungicidal seed treatment contain about 98% HCB and 1.8% pentachloronitrobenzene (PCNB). Commercial dusts for similar purposes contain 10-40% HCB and 0.5 to 1.0% Lindane. In 1971, such uses consumed 15,000 pounds of HCB.

Dacthal is popular with homeowners for lawns and gardens. Large quantities are applied by commercial growers to onions, cabbage, strawberries, and vegetable seeds; smaller amounts are used on soybeans, green peppers, cotton, snap beans, Irish potatoes, watermelon, and other crops.

PCNB is used for cotton, peanuts, and nectarines, and in nurseries. It is also added to fertilizer and sold to ranchers and homeowners in this form.

The possibility that HCB could reach the environment from industrial installations, as in Louisiana, raises some serious questions. A number of industrial processes can release HCB, including those for manufacture of chlorine gas, perchlorethylene, carbon tetrachloride, and other chlorinated hydrocarbons. Available information suggests that the plants in Louisiana followed common industrial practices for control and disposal of waste HCB; there is no reason to believe that the problem resulted from failure to follow normal procedures or from accidents leading to discharge of HCB. There, therefore, exists the possibility, even the likelihood, that similar problems could appear in the vicinity of any installation using the same technology.

Hexachlorobenzene is formed during the reaction of chlorine and hydrocarbons at a temperature greater than 150°C (300°F). HCB is a normal byproduct of perchlorethylene and carbon tetrachloride production, chlorine production using graphite anodes and mercury cathodes and other hydrocarbon chlorination processes. The tarry residue "hex" waste from perchlorethylene and carbon tetrachloride production is reported to contain 10-15% HCB, 70-75% hexachlorobutadiene (HCBD), and 10-20% hexachloroethane. (Dow; Vulcan).

Hexachlorobenzene as byproduct could possibly be emitted directly into the air from processes which produce HCB.

Improper containment during transport of "hex" waste can result in contamination as HCB can enter the air via sublimation, or appear as a dust which can contaminate soil and water and settle onto vegetation surfaces.

Certain means of disposal of "hex" waste such as dumping in a landfill can lead to migration via water and sublimation into the air. HCB has been detected in the air at the Ascension Parish Landfill in Louisiana where "hex" waste is known to have been dumped (air concentrations ranged from 13-14 ppb or 16-18 $\mu g/m^3$). (Enos, EPA, 1973)

Only a limited amount of work has been directed toward the development of environmentally sound disposal methods for "hex" wastes and other HCB-containing waste streams.

The Dow Chemical Co. has been using a "thermal oxidizer" (a steam-oxygen feed incinerator) for disposal of their "hex" waste. Dow's production manager at the Louisiana Division in Plaquemine stated that the products of incineration are water, hydrogen chloride, and carbon dioxide and that the scrubbing process is better than 99% efficient. This incinerator is more or less a prototype and Dow does not feel it is marketable technology in its present form. Further development at present involves the quenching of hot gases, the design of the burner nozzle, and materials of construction. Recycling of hydrogen chloride using a water scrubber is a possibility which has not yet been exploited. Dow claims that at capacity total loss of "hex" waste to air and water is about 10 pounds per day, thus HCB loss is about 1 pound/day. The environmental adequacy of this treatment should be determined.

Landfill disposal is used by many chemical manufacturers for "hex" waste disposal. This method of disposal seems questionable from an environmental standpoint.

Plants of the types that can produce HCB are scattered throughout the country, and there are several concentrations of plants similar to the Geismar complex. The locations of these plants are currently being plotted, and plans have been proposed for concentrating HCB surveillance activities in the areas of such facilities.

Problems of contamination with HCB are not limited to the United States. Residues of HCB in human tissue have been found in studies in Australia, Japan, and Germany. At least one country, New Zealand, has completely banned the use of HCB.

Hams from the Netherlands and cheeses from several European countries have been refused entry into this country because of excessive HCB levels. Australia and the United Kingdom have also found high HCB levels in cheese and grain imported into those countries.

World-wide concern with HCB became serious enough to warrant consideration of the problem by the World Health Organization (WHO). In 1969, WHO proposed interim recommendations for HCB tolerances in a number of foodstuffs, including 1.0 ppm in the fat of meat and poultry, 0.3 ppm in fat content of dairy products, 0.01 ppm in cereal products, and 1.0 ppm in eggs (shellfree basis). It was recognized at that time that sufficient information on the effects of HCB was not available. Unfortunately, little more is known now than was known then, although a few studies have been conducted, mainly in the United States and New Zealand. The WHO recommendations expired on July 1, 1973, and have not been extended.

Chemistry and Analysis of Hexachlorobenzene

Hexachlorobenzene can be encountered in a number of forms, including crystals, powder, vapor, suspended particulates in either air or water, and dissolved in related organic materials.

All evidence, at present, indicates HCB to be a very stable, unreactive compound, even under relatively severe laboratory conditions. Physical and/or chemical degradation has not been shown to occur. Worthy of note, however, is that HCB is volatile in water vapor even at low temperatures. Such co-distillation or vaporization provides a physical mechanism for environmental dispersal of HCB. It also sublimes readily, and will evaporate if exposed to air under conditions of adequate ventilation.

Hexachlorobenzene (C_6Cl_6) should not be confused with "benzene hexachloride" (Lindane, BHC), which is actually hexachlorocyclohexane ($C_6H_6Cl_6$).

Physical properties are shown in table I.

Table I

Chemical Structure

(1) Hexachlorobenzene (also known as HCB and perchlorobenzene) C_6Cl_6

Physical properties of pure material (Kirk-Othmer (1966); Hawley (1971))

(1)	boiling point	326°C
(2)	melting point	229°C
(3)	flash point	468°F
(4)	solubility	insoluble in H_2O
(5)	vapor pressure	1.089×10^{-5} mm Hg at 20°C
(6)	appearance	colorless (white) powder or colorless needles

Procedures for analyzing for HCB in air, water, soil, vegetation, and fatty tissue have been developed and are being used by FDA, USDA, and EPA. The preferred method of analysis is by gas chromatography with mass spectrometric verification of HCB.

Problems with collection of air samples for HCB analysis were noted by the EPA Perrine laboratory at the inception of the current activity. The standard technique using ethylene-glycol impingers did not give samples that accurately reflected the amount of HCB in the air. A new technique for collecting samples was developed and is now being used by the State of Louisiana and by Region VI.

Older procedures for analysis of chlorinated hydrocarbon residues did not distinguish between HCB and the alpha isomer of benzene hexachloride. Consequently, many of the older reports of both HCB and α-BHC must be considered suspect. Procedures now in use do make this distinction, however.

Toxicology Aspects of Hexachlorobenzene

Human Health Aspects

An outbreak of porphyria cutanea tarda in southeastern Turkey in 1955 was traced to the inadvertent consumption of HCB-contaminated seed grain (wheat) distributed by the Turkish government for planting purposes. Estimates of the total number of cases over a five-year period are from 3000-5000 with approximately 80 percent of the cases in children 4-14 years of age. The estimated dose was approximately 50 to 200 mg/day for a presumably long period of time before manifestations of the disease became apparent. (Schmid, R., 1960; Cam, Nigogosyan 1963)

Clinical manifestations observed included:

a. blistering and epidermolysis of the skin in areas exposed to sunlight, particularly face and hands.

b. poor healing of these lesions

c. hyperpigmentation (discoloration of skin) accompanied by hypertrichosis (excess hair) which was not limited to the exposed skin areas

d. urine containing large quantities of porphyrins

e. hepatomegaly (liver enlargement) in approximately 35 percent of the cases

f. weight loss

g. in some cases, osteoporosis (bone deterioration) of extremities and interphalange (fingers or toes) arthritis

h. thyroid enlargement in 30 percent of cases, but no signs or symptoms of hyperfunction

i. enlargement of lymph nodes

Acute skin manifestations disappeared within 20 to 30 days after discontinuation of intake of HCB. However, relapses were

often seen during the summer months. A predilection of the disease for males was observed (about 76 percent of cases). (Cam and Nigogosyan, 1963).

An Australian study of occupationally exposed individuals showed levels in blood ranging from 0 to 410 ppb. A control group with no known exposure showed blood levels ranging from 0 to 95 ppb. HCB was detected in 95 percent of the people tested (the minimum detectable level was 10 ppb). No toxic effects were reported. (Brady, 1372).

Another Australian study of a random selection of perirenal fat samples taken at autopsy revealed 100 percent positive samples with levels from "trace" to 8.2 ppm; 33 percent of the samples contained greater than 1 ppm. The mean for all samples was 1.25 ppm. No toxic effects were reported. (Brady & Siyali, 1972).

A German study detected residues in human fat of 6.3 ppm and 5.3 ppm in human milk. No toxic effects were reported. (Acker, and Schulte, 1971).

A recent Japanese study has shown levels in human adipose tissue to range from 0.30 to 1.48 ppm. No toxic effects were reported. (Curley, et al., 1973).

Animal Studies

A 90-day feeding study was performed in 1962 by the Hazleton Laboratories for the Diamond Alkali Company. Rats were fed diets containing HCB at levels of 0,5,25,125, and 625 ppm for 13 weeks. There were no deaths reported at any dose level.

At 625 ppm the rats displayed signs of marked respiratory involvement and slight tremors which were not observed at any of the other dose levels. The 625 ppm group also showed reduced growth rate, elevated total leukocyte counts and increased organ weights in liver, spleen, and adrenals. Microscopic examination showed consistent adverse effects in the liver. At the 125 ppm level, liver weight increased and microscopic examinations showed adverse effects in the liver. In addition, at both the 125 ppm and 625 ppm levels, some less distinct and inconsistent changes were observed in thyroid, kidneys, adrenals, and bone-marrow. At 5 and 25 ppm, no significant effects were observed in organs and tissues.

In a study by the Dow Chemical Company (Kociba, et al., 1971) HCB was fed in feed to female weanling rats for 30 days. Doses ranged from 1 to 100 mg/kg/day (0, 1, 3, 10, 30, 65, 100). Rats at 30, 65, and 100 mg/kg/day dose levels showed gross and histopathologic alterations in the liver. Examination of tissues from the 1, 3, and 10 mg/kg/day rats showed no definitive pathological changes.

Administration of HCB at 5000 parts per million to two female rats (De Matteis et al 1961) showed apparent excretion of HCB and/or its metabolites in milk. One animal died, but the other delivered normally and reared the young until they died with convulsions after 7 to 8 days. She was then placed with three normal week-old pups to foster. The pups died 3 to 4 days later exhibiting convulsive seizures, and the foster mother died similarly 4 weeks later.

Other animal studies are summarized in Tables II and III.

Bioaccumulation

Hexachlorobenzene has been shown to be quite stable even under severe laboratory test conditions. (Allis, EPA, 1973). It apparently undergoes relatively little biotransformation, or degradation and is thus a highly persistent chemical. Residues have been detected in foods, various organisms (wild and domestic) including man, and various media. Detectable levels have been found in municipal water supplies in Louisiana and Indiana (EPA report, 1972).

Tissue residue data have revealed that HCB will bioconcentrate and indicates potential biomagnification up the food chain, since predatory birds have been found with detectable levels of HCB (Zitco and Choi, 1972); Gilbertson and Reynolds, 1972).

Experimentally, in sheep the storage of HCB in body fat is 7 to 9 times the concentration in feed at all levels of intake from 0.1 ppm to 100 ppm. (Avrahami and Steele, 1972).

In the chicken, HCB can accumulate in the body fat to at least 20 times the concentration fed in the diet. (Avrahami and Steele, 1972).

Studies by Metcalf, et al., in model ecosystems showed bioconcentration of HCB by algae, snails, mosquitoes, water fleas, and fish to part-per-million levels while in an aquatic environment with 3 ppb HCB. (Metcalf, 1973, in press).

Table II

ACUTE TOXICITY OF HEXACHLOROBENZENE FOLLOWING SINGLE DOSE ORAL ADMINISTRATION, MG/KG[1]

Species	Minimum Toxic Dose[2]	Minimum Lethal Dose	Average Lethal Dose	Absolute Lethal Dose
Mice	400	2000	about 4000	about 7500
Rats	500	2000	3500	6000
Rabbits			2600	
Cats			about 1700	
Guinea pig[3]			1000	

[1] Savitskii, 1964.

[2] The signs of intoxication associated with a minimum toxic dose were not described.

[3] Mellis, (1955)

TABLE III (Cont)

Route	Species	# Animals	Sex	Dose	Duration	Observations
Oral[5](Continued)						symptoms. Decreased egg production and hatchability. Porphyria. Increased liver wt. Liver and kidney pathology.
Oral[6]	Guinea Pig	X	X	X	8-10 days	marked neurological symptoms--tremors, convulsions, death
	Mouse	X	X	X	8-10 days	
0.5% in feed	Rabbit	X	F	X	6 weeks 8-12 weeks	increased urinary porphyrins tremors, paralysis, death
Inhalation[2] 0.03 mg/l	Rabbit	X	X	X	daily exposure	alteration of red blood cell and hemoglobin content of the blood
Inhalation[2] 0.009 mg/l	Rabbit and Cat	X	X	X	68-78 daily exposure	no apparent effects
Oral[7] (in feed 60% HCB) commercial fungicide	Sheep 1 yr old (22-24 kg) food consumption about 1 kg/day	5	F	0.1 mg HCB day(.1ppm)	18 weeks	no apparent effects
		5	F	1 mg HCB day (1 ppm)		
		5	F	10 mg HCB day (10ppm)		
		5	F	100 mg HCB day(100ppm)	18 weeks	1/3 reduction in growth rate
Oral[7] in feed (60% HCB in commercial fungicide)	Chicken 12 days old	20	F	0.1,1,10,100 mg/day	180 days	no apparent effects
	Chicken - 8 mo. old egg laying	20	F	0.1,1,10,100 mg/day	180 days	no apparent effects on birds, or fertility or hatchability of eggs.

[1]Unpublished data. The Dow Chemical Company.

[2]Ockner and Schmid (1961)

[3]Savitskii (1964)

[4]Gurfein and Pavlova (1960)

[5]Vos, et al (1971)

[6]DeMatteis, et al (1961)

[7]Avrahami and Steele (1972)

[X]Information not given in paper

TABLE III

SUBACUTE AND CHRONIC TOXICITY OF HEXACHLOROBENZENE

Route	Species	# Animals	Sex	Dose	Duration	Observations
Oral[1] (in feed)	Rats	5	M	2 mg/kg/day	13 days	No toxic effects.
		5	M	6 mg/kg/day		Very slight skin twitching and nervousness. Significant inc. in liver weight.
		5	M	20 mg/kg/day		Neurotoxic symptoms. Increase in liver weight.
		5	M	60 mg/kg/day		Neurotoxic symptoms. Increase in liver and kidney weights.
		5	M	200 mg/kg/day		Neurotoxic symptoms. Increase in liver and kidney weights.
Oral[2] (in feed)	Rats	33		100 mg/kg/day	51 days	13 deaths in one month. Neurotoxic symptoms. Increased liver weight Porphyria.
Oral[3] (in feed)	Rats	10		300 mg/kg/day	10 days	30% mortality
		10		150 mg/kg/day	30 days	60% mortality
		10		50 mg/kg/day	30 days	30% mortality
Oral[4] (in water)	Rats	13		0.025 mg/kg/day	4-8 mos.	No toxic symptoms. Possible effect on conditioned reflexes.
Oral[5] (in feed)	Quail	3 males and 12 females (per feeding rate)		0.1 mg/kg/day	90 days	No toxic effects.
				0.5 mg/kg/day		Slight increase in liver weight. Minimal liver pathology and porphyria.
				1.8 mg/kg/day		Increased liver wt. Liver and kidney path. Decreased egg production. Porphyria.
				7.2 mg/kg/day		5 (4 females & 1 male) deaths-18 to 62 day period. Neurotoxic

Guidelines for Permissible Residue Levels

In response to a request from USDA, EPA reviewed available data on the toxicology of HCB, and concluded that it was not adequate to permit establishment of a tolerance level for HCB in food. This was confirmed by consultations with scientists in USDA and the Department of Health, Education, and Welfare, and with members of the scientific community.

Nevertheless, HCB occurs in food frequently enough that some guidance is necessary to protect public health. The experience in Turkey vividly demonstrates the health effects of HCB when ingested over a long period. There is, however, no experience which indicates the effects of low doses on humans. Attempts in the United States and abroad to determine the safe level of HCB in experimental animals have been extremely limited and sporadic, and at present there is a lack of authoritative data. Experiments on a variety of animals have been limited in design, scope, and duration. Meaningful inferences are difficult to draw although there are indications that repeated dosages of HCB at low levels may be harmful.

Related to these uncertainties is the unknown extent which meat products with low levels of HCB residues are likely to reach individual consumers on a repetitive basis. The sources of HCB of immediate concern are confined to very small geographic pockets which traditionally disperse a significant portion of their products to markets around the country.

Similarly, little information is available for assessing the economic impact of alternative tolerance levels. In the original Louisiana quarantine area, for example, there were up to 20,000 food animals with HCB in their fat at levels ranging from 0.1 to 6.0 ppm. However, the extent that these levels could be reduced through fattening with clean feed and through natural processes prior to slaughter is uncertain. Similarly, the cost and success of biochemical methods to reduce the levels are difficult to assess. There are many other economic costs related to establishing a tolerance including the impact on the value of contaminated land, the costs of alternative feed supplies and the long-term impact on animal herds. Data are not available to assess these types of impact. Furthermore, the extent and levels of HCB residues which will appear in the months and years ahead in many areas of the country cannot be predicted.

An analysis of some of the short-term economic implications of various tolerance levels is given in Table IV. The analysis considers only direct short-term cattle losses and does not address many other implications related to factors such as land values, longer term cattle losses and costs of feed. Data are not available for such analyses at this time.

On June 1, 1973, EPA recommended an interim action guideline of 0.5 ppm HCB in fat of cattle, swine, sheep, horses, and goats at the time of slaughter. This is based on analysis of the best data available, including toxicological studies and economic considerations. The recommended guideline is designed to protect the consumer under any reasonable set of assumptions concerning the likelihood that meat with the maximum allowable level of HCB will be continuously consumed. The guideline will be reviewed every 90 days with the view to establishing a tolerance within three years should adequate technical data become available. If sufficient technical data are developed in the meantime which indicate a need to alter the guideline, the guideline will be adjusted accordingly.

The Food and Drug Administration, taking into account similar considerations, has adopted an interim guideline of 0.3 ppm HCB residues in fat for milk and dairy products.

At present, no guideline exists for HCB residues in poultry or eggs.

TABLE IV

Economic Effects of Various Guideline Levels on Cattle in the Geismar Area
(based on data to May 31, 1973)

Level (ppm)	%	and no. of cattle above level	%	and no. of cattle above level assuming dilution factor of: 2:1		3:1		4:1		6:1
0.3	36%	11,700	22%	7,150	17%	5,525	16%	5,200	12%	3,900
0.5	24%	7,800	17%	5,525	14%	4,550	11%	3,575	7%	2,275
1.0	17%	5,525	11%	3,575	7%	2,275	2%	650	0.7%	288
1.5	14%	4,550	7%	2,275	2%	650	0.7%	228	___	___

NEAR TERM CATTLE LOSSES
(in millions)

Level	Assuming no dilution	Assuming dilution factor of: 2:1	3:1	4:1	6:1
0.3	$5.85	$3.58	$2.76	$2.60	$1.95
0.5	$3.90	$2.78	$2.28	$1.79	$1.14
1.0	$2.76	$1.79	$1.14	$ .33	$ .11
1.5	$2.28	$1.14	$ .33	$ .11	___

N.B. See text (p. 20) for assumptions used in calculating these figures.

Conclusions and Current Activity

The following conclusions seem consistent with the minimal data available on HCB.

HCB is a compound of low acute toxicity, but significantly higher subacute toxicity. Available toxicological data indicates that, while a single large dose may have no lasting effects, repeated administration of much smaller doses over periods ranging from ten to ninety days can result in serious physiological effects.

The material is very stable and defies metabolic and/or environmental degradation. It is known to bioaccumulate in cattle, sheep, and other animals. Preliminary studies suggest it will also bioconcentrate in food chains.

Sources of contamination are not limited to pesticidal use or misuse. Indications are that industrial sources may be a significant factor in at least one situation in this country with many more areas exhibiting the potential for such contamination. The situation which has precipitated the present concern does not appear to be the result of a unique set of circumstances.

The persistence of HCB and its demonstrated high toxicity at repeated low level doses in animal studies justifies a high level of concern with regard to the residue which should be permitted to accumulate in any segment of the environment (food, biota, man, air, water, soil) and the overall hazard posed to the total environment.

The following activities to be carried out by the Environmental Protection Agency and other concerned Federal and State agencies are planned or already underway:

Toxicological Research

1. A lifetime feeding study in rats to improve understanding of the effects of long-term exposure to low level dosages of HCB. This study is underway at the USDA laboratory in College Station, Texas.

2. A three-generation reproduction study in rats to provide a measure of the effects of HCB on growth and reproduction. This study is underway at the EPA laboratory in Chamblee, Georgia.

Epidemiological Research

3. A study of human populations in a limited geographical area to determine if effects characteristic of HCB intoxication are present. This will include analysis of blood for HCB and for ALA enzyme activity and of urine for porphyrin content.

4. A similar study of workers in factories producing chlorinated hydrocarbons (tentative).

Other Research

5. A study of the effects of various methods to reduce HCB levels in the tissues of living animals, including natural and drug-induced elimination, and analyses of the dilution of HCB in fat during normal growth of a young animal.

6. Development of improved methodology and techniques for detection, collection, and analysis of HCB in air. This work is underway at the EPA laboratory in Perrine, Florida.

Monitoring

7. Monitoring of air, water, soil, and vegetation in the Geismar area in order to assist in identifying the source of HCB contamination in that area. This effort is being done by the State of Louisiana and by EPA.

8. Monitoring of air and soil in the neighborhood of other industrial complexes were chlorinated materials are produced to determine if HCB is being released to the environment. This activity is being initiated in Louisiana and Texas by EPA Region VI, and may be expanded to other regions if it appears desirable to do so.

9. Analysis for HCB residues of samples of soil, water, plants and tissues (human and animal) collected in nationwide pesticide monitoring activities. This work will be done initially at the EPA laboratory at Bay St. Louis, Mississippi.

10. Analysis of samples collected under 7, 8, and 9 above for hexachlorobutadiene (HCBD) which is another potential problem. Also, its occurrence with HCB assists in determining if industrial waste is the source of HCB in specific areas.

Control Technology

11. Review of methods being used to control wastes containing HCB and evaluation of their environmental safety.

12. A study of the effects of disposing of industrial wastes containing HCB in sanitary landfills.

Other

13. A review of the use of registered pesticides known to contain HCB (Dacthal and PCNB) to determine if their uses could lead to hazardous environmental levels of HCB.

14. Referral of available toxicological data on HCB to an expert scientific advisory group (the Hazardous Materials Advisory Committee) for review and recommendations.

15. A study of the economic impact of various tolerance levels for HCB in food, including effects on the food supply and on farmers and ranchers.

16. A nationwide analysis of the potential industrial sources of HCB and related compounds of particular concern.

17. Systematic analyses by FDA for HCB in the following sampling programs: market basket surveys, surveillance of raw agricultural products, and surveillance of imported products.

Additional activities which might be considered include the following:

1. A study to determine the levels of HCB which produce in animals the biochemical aberrations associated with porphyria cutanea tarda (the syndrome observed in Turkey). This would be especially valuable since the earliest clinical manifestation of HCB poisoning in man appears to be hyperphotosensitization, an effect which cannot be observed with laboratory animals.

2. Metabolic studies in animals, including identification of the substance responsible for fatalities in nursing animals when the nurse is fed HCB. (This substance could be HCB itself, but this has not been demonstrated.)

3. A study of the teratogenic potential of HCB.

4. A study of the mutagenic potential of HCB.

5. Development of environmentally acceptable and economically practical methods for disposal of "hex" wastes. Problems with HCB are bound to recur until this is done.

Bibliography

Acker, L., and Schulte, E. (Organochlorine Compounds in the Human Body) Umschau 71 (23), 848 (1971).

Allis, J.W. - EPA-ORM-Molecular Biology Branch (May 1973)

Avrahami, M., and Steele, R. T.
Hexachlorobenzene I. Accumulation and Elimination of HCB in Sheep after Oral Dosing. N.Z.J. Agr. Res. 15 (3), 476-481 (1972)

Hexachlorobenzene II. Residues in Laying Pullets Fed HCB in Their Diet and the Effects on Egg Production, Egg Hatchability, and on Chickens. N.Z.J. Agr. Res. 15 (3), 480-488 (1972)

Hexachlorobenzene III. The Effects of Feeding HCB to Growing Chickens. N.Z.J. Agr. Res. 15 (3), 489-494 (1972)

Brady, M. N. and Siyali, D. S., Hexachlorobenzene in Human Body Fat. Med. J. Aust. (1972) 1, 158-161.

Cam, C. & Nygogosyan, G., Acquired Porphyrin Cutanea Tarda due to Hexachlorobenzene. J. Am. Med. Assoc., 183, 88-91 (1963)

Curley, et al., Nature 242, 333 (1973)

DeMatteis, F. et al. Nervous and Biochemical Disturbance following Hexachlorobenzene Intoxication. Nature 191, 363-6 (1961)

Dow Chemical Co., Plaquemine, La. personal communication (May 1973)

Enos, H., EPA-Perrine Laboratory (May 1973)

EPA (1972) report - "Industrial Pollution of the Lower Missippi River in Louisiana, April 1972". - Indiana - (Evansville) - communication with Dr. R. Tardiff-EPA-Water Supply Research Lab., Cincinnati

Gilbertson, M., and Reynolds, L.M., (1972) Bulletin of Env. Contamination and Toxicology Vol. 7, No. 6

Gurfein, L.N. and Pavlova, Z.K. Maximum allowable concentration of chlorinated benzones in water reservoirs. Sanitarnaya Okhrana Vodoemov of Zagryazneniya Promyshlennymi Stochnymi Vodami. No. 4: 117-127, (1960)

Hawley, G.G., Ed. Condensed Chemical Dictionary, 8th ed. Van Nostrand Rheinhold (1971)

Kirk-Othmer, Encylopedia of Chemical Technology, 2nd Ed., Interscience (1966)

Kociba, R. J. , et al. Toxicologic study of Female Rats Administered Hexachlorobutadiene or Hexachlorobenzene for Thirty Days. Dow Chemical Co. Midland, Mich., Aug. 27 (1971)

Melis, R. Toxic Action of Hexachlorobenzene for Warm-blooded Animals. Nuovi Ann. Ig. 6, 361-7 (1955) (chem. Abstr.) 50, 5170g (1956)

Metcalf, R. L., "Model Ecosystem studies of the environmental fate of six organochlorine pesticides", in press, Env. Health Perspectives (1973).

Ockner, R. K. and Schmid, R. Acquired porphyria in man and rat due to hexachlorobenzene intoxication. Nature 189:499, (1961)

Savitskii, I.U., The Basis for Determining Safe Permissible Concentrations of Hexachlorobenzene and Pentachloronitrobenzene in the Air. (Russian) Vopr. Prom. i. Selskokhozyaistrennoi Toksikologii Kievsk, Med. Inst. 158-173 (1964) (Chem. Abstr. 63, 8952d (1965)

Schmid, R. Cutaneous Porphyria in Turkey. New England J. Med., 263, 397-398 (1960)

Vulcan Materials Co, Geismar, La. personal communication (May 1973)

Weir, R. J., Experimental Pre-Emergence Herbicide HCB pure (new), 90-day dietary Administration - Rats. Unpub. Report of Hazleton Laboratories, Inc. Sponsored by Diamond Alkali Co. (1962)

Zitco, V. and Choi, P.M.K. (1972), PCB, and p,p -DDE in Eggs of Cormorants, Gulls, and Ducks from the Bay of Fundy, Canada, Bulletin of Env. Contamination and Toxicology Vol. 7, No. 1.